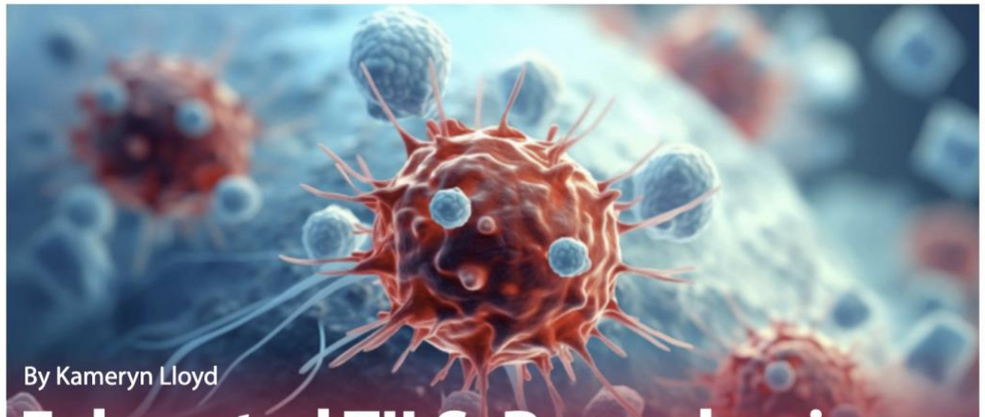


By Kameryn Lloyd

Exhausted TILS: Reawakening Cancer-Fighting T-cells

Have you ever been so stressed you can barely function? Well, you and T-cells have something in common. Tumor-infiltrating lymphocytes (TILs) are a specific type of immune T cell whose job is to locate and kill cancer cells. However, these cells can become exhausted leading to less response to immunotherapies allowing for tumors to continue to grow. Dr Jessica Thaxton an associate professor in the Department of Cell Biology and Physiology and her lab members are working together to target T-cell exhaustion, improving immunotherapy response and shrinking tumors.

Dr. Jessica Thaxton

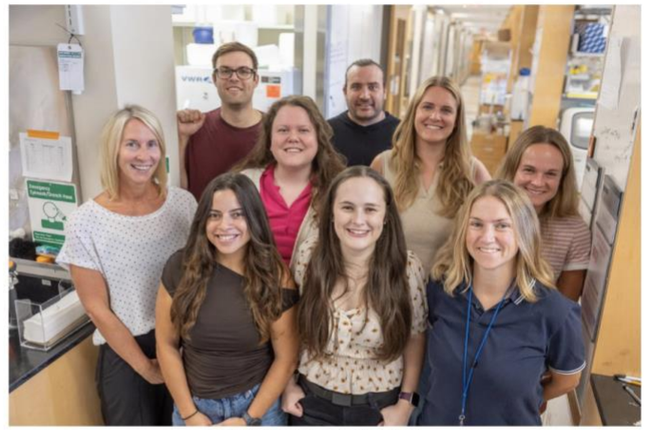
All cells have a stress response which is a way to alert themselves that something is wrong or off-balance in the body. "It is just like when you become stressed." Whether it be yoga or meditation. Every person has ways to cope with and relieve the stress in our lives and so do our immune cells. However in tumors, no matter how the immune cells try to respond and bring themselves back to their normal state, the stress can't be relieved. This causes them to become exhausted and subsequently less effective at targeting and shrinking tumors. Similarly to a yoga instructor or a therapist, the goal of Dr. Thaxton's lab is to bring these immune cells experiencing the high-stress environment of tumors back to their normal homeostatic state.

Dr . Thaxton's lab found that the main driver for the T-cell stress response was the Endoplasmic reticulum (ER). Her lab is separated into three groups all working towards targeting ER stress in different ways. One way is to target the molecules that alert the cell to the stress in the body. By tuning these molecules up and down they can limit the amount of stress signaling the T-cells are receiving. However, these molecules can be difficult to target as they are important for other cells in the body. One of the methods they use to further this goal is RNA-seq. This technique allows the lab to examine all of the RNA sequences in a cell, which gives insight into the genetic components. The 2nd group has found that after the stress response starts there's a drastic increase in metabolism in the T cell. Their goal is to find ways to get the cells more energy so that they can work harder and longer. One technique they are using to understand this is spectral flow cytometry. This is done by using metabolic dyes that become fluorescent tags for parts of the cell's metabolism like glucose or fats. This allows them to compare the energy uptake in the TILs to other T-cells in the body. The third group has found that when the cells become stressed it causes the Endoplasmic Reticulum to change shape. Their goal is to target the ER structure in order to improve immune cell functioning. One method used to better understand ER structure is using imaging from a confocal microscope. This allows them to visualize the T-cells Endoplasmic Reticulum and better characterize the shape changes.

"My passion is to get the work we're doing at the bench to directly translate to the bedside". Dr. Thaxton's end goal is to have her work become translational and help treat cancer patients. To accomplish this, her lab collaborates with clinicians. They work closely with multiple surgical oncologists to better compare if the stress responses seen in mouse models are also being seen in patients. Mouse models can also be improved by comparing the stress environment in the mice to the human sample. Working with patient samples will make it easier to bridge the gap between creating therapeutics that are equally as effective in mice and humans. Subsequently, the results from the collaboration have found that many of their discoveries found in mouse models do match patient tumors. However, there have been barriers that have made translation difficult. One of which is toxicity, it is challenging to find a unique drug target that does not cause harm to other cells and tissue. They have discovered one non-toxic target that has shown success. However, another barrier is finding pharmaceutical companies to source their therapeutics that are also prepared to enter clinical trials. These and many other obstacles continue even after discoveries in the lab are made.

"My passion is to get the work we're doing at the bench to directly translate to the bedside."

One of the things Dr Thaxton is excited about looking toward the future of her project is working with and continuing to mentor her lab members. She has seen how each member's unique background and perspective have helped make the projects thrive. The lab is also working towards a future grant with her clinical partners that would allow them to have a project that solely focuses on using patient samples. Another project she is excited about is the non-toxic drug candidate discussed earlier and its possibilities in in-patient clinical testing. While research can sound difficult Dr. Thaxton reminds undergrads to "always follow the science that you love" and not be intimidated as most research can be boiled down into simple questions. Dr. Thaxton's questions on the relationship between T-cells and stress could transform cancer treatments and save patient's lives.



Members of the Thaxton Lab

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